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Chronic pelvic pain treated with gabapentin and amitriptyline: A randomized controlled pilot study

Sabine M. Sator-Katzenschlager[1], **Gisela Scharbert**[1], **H■■■ G. Kress**[1], **N■■■ Frickey**[1], **A■■■ Ellend**[2], **A■■■ Gleiss**[3], and **Sibylle A. Kozek-Langenecker**[1]

[1] Department of Anesthesiology and Intensive Care (B), Pain Clinic, Medical University of Vienna, Vienna, Austria
[2] Department of Gynecology and Obstetrics, Medical University of Vienna, Vienna, Austria
[3] Core Unit for Medical Statistics and Informatics, Medical University of Vienna, Vienna, Austria

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Zusammenfassung. *Einleitung:* Gegenstand der Studie war der Vergleich der Wirksamkeit und Verträglichkeit von Gabapentin bzw. Amitriptylin allein mit der Kombination der beiden Medikamente bei chronischen Unterbauchschmerzen (chronic pelvic pain, CPP).

Methoden: 56 weibliche Patientinnen mit chronischen Unterbauschmerzen wurden bei der prospektiven, randomisierten open-label-Studie mit einem 2-jährigem follow-up an der Schmerzambulanz der Universitätsklinik Wien, Österreich, eingeschlossen. Wenn die Schmerzintensität trotz analgetischer Therapie mit dem Nichtopioid Metamizol und einem schwachen Opioid gemessen auf der visuellen Analogskala (VAS) bei 5 oder darüber lag (0 = kein Schmerz, 10 = schlimmster vorstellbarer Schmerz), wurden die Patientinnen randomisiert einem der drei Behandlungsarme zugeteilt (Gabapentin, n = 20; Amitriptylin, n = 20 oder beides, n = 16). Die Medikamentengaben von Gabapentin bzw. Amitriptylin wurden auf eine tägliche Dosis von 3600 mg bzw. 150 mg gesteigert, bis eine suffiziente Schmerzerleichterung erreicht war oder unerwünschte Nebenwirkungen auftraten. VAS-Werte wurde vor Beginn der Behandlung und 1, 3, 6, 12 und 24 Monate danach erhoben.

Ergebnisse: Alle Patientinnen erfuhren während des Beobachtungszeitraumes eine signifikante Schmerzreduktion. Dennoch war die Schmerzreduktion bei Patientinnen, die Gabapentin allein oder in Kombination mit Amitriptylin erhalten hatten, signifikant höher als unter Monotherapie mit Amitriptylin (Gabapentin: 0: 7.7 ± 1.5, 6: 1.6 ± 0.9, 12: 1.5 ± 0.9, 24: 1.9 ± 0.9; Amitriptylin: 0: 7.3 ± 1.5, 6 : 2.2 ± 1.6, 12: 2.2 ± 1.6, 24: 3.4 ± 0.9; Amitriptylin/Gabapentin: 0: 7.6 ± 0.8, 6: 1.3 ± 0.9, 12: 1.7 ± 1.0, 24: 2.3 ± 0.9). Unerwünschte Nebenwirkungen traten signifikant seltener in der Gabapentin-Gruppe auf als in den beiden anderen Gruppen ($p < 0.05$).

Konklusion: Diese Ergebnisse legen nahe, dass die Pharmakotherapie mit dem Antikonvulsivum Gabapentin die Behandlung von chronischen Unterbauchschmerzen bei ambulanten Patientinnen verbessert.

Summary. *Background:* The aim of this study was to compare the efficacy and side effects of gabapentin, amitriptyline, and their combination in women with chronic pelvic pain.

Methods: In this open-label, prospective, randomized trial 56 women with chronic pelvic pain were investigated with a two-year follow-up at the Vienna medical university hospital. If pain intensity assessed by a visual analog scale (VAS) was 5 or more (0 = no pain, 10 = maximal pain), despite analgesic therapy using the nonopioid drug metamizol together with weak opioids, patients were randomized to receive gabapentin (n = 20), amitriptyline (n = 20), or a combination of both drugs (n = 16). Doses of gabapentin and amitriptyline were increased to maximum daily doses of 3600 mg and 150 mg, respectively, until sufficient pain relief or the occurrence of side effects. VAS and side effects were evaluated before treatment and at 1, 3, 6, 12 and 24 months afterwards.

Results: All patients experienced significant pain relief during the observation period. However, after 6, 12 and 24 months, pain relief was significantly better in patients receiving gabapentin either alone or in combination with amitriptyline than in patients receiving monotherapy with amitriptyline (gabapentin: 0 months: 7.7 ± 1.5, 6 months: 1.6 ± 0.9, 12 months: 1.5 ± 0.9, 24 months: 1.9 ± 0.9; amitriptyline: 0 months: 7.3 ± 1.5, 6 months: 2.2 ± 1.6, 12 months: 2.2 ± 1.6, 24 months: 3.4 ± 0.9; amitriptyline/gabapentin: 0 months: 7.6 ± 0.8, 6 months: 1.3 ± 0.9, 12 months: 1.7 ± 1.0, 24 months: 2.3 ± 0.9). Side effects were lower in the gabapentin group than in the two other groups, the difference reaching statistical significance after three months ($P < 0.05$).

Conclusion: Gabapentin alone or in combination with amitriptyline is better than amitriptyline alone in the treatment of female chronic pelvic pain.

Key words: Chronic pelvic pain, gabapentin, amitriptyline.

Introduction

Pelvic pain in women may be induced by gynecological, urological, gastrointestinal, musculoskeletal or psychiatric pathologies [1], and can be of visceral and/or neuropathic origin [2–5]. Recommended state-of-the-art treatments for visceral and neuropathic pain differ considerably [4, 7–9]. Tricyclic antidepressants and anticonvulsive drugs have emerged as effective standard treatment options for neuropathic pain [6]: amitriptyline is an effective tricyclic antidepressant, but side effects often limit its clinical use [10, 11]; gabapentin [1-(aminomethyl)cyclohexanacetic acid] is a structural analog of γ-aminobutyric acid, which was initially introduced in 1994 as an anticonvulsive drug [12–14], and has been reported to be well tolerated and effective in the treatment of various chronic pain conditions, particularly in neuropathic pain [13, 15]. To date, no study has determined the efficacy and safety of antineuropathic therapy in patients with chronic pelvic pain. Accordingly, we compared the effects of amitriptyline and gabapentin and their combination in women with chronic pelvic pain refractory to antinociceptive treatment for visceral pain.

Materials and methods

Women consecutively entering treatment for chronic pelvic pain persisting longer than six months were enrolled in this study at our outpatient pain center between October 2000 and October 2002. Local ethics committee approval was obtained and patients provided informed consent to their participation prior to data analysis. Before beginning treatment, patients underwent detailed and standardized gynecological, urological, neurological, internal and psychological evaluation according to the protocol of our outpatient pain center.

First-line pain therapy consisted of 1000 mg metamizol four times daily, together with 100 mg of the weak opioid tramadol twice daily, and with rescue medication tramadol 50 mg up to six times daily (Fig. 1). Pain intensity was scored using a visual analog scale (VAS; 0 = no pain, 10 = worst pain imaginable). The quality of pain was described by the patient as burning, lancinating, electrifying or searing (neuropathic pain), or a combination of neuropathic and nociceptive pain qualities (dull, aching, cramping, vice-like sensations: i.e. nociceptive pain of somatic or visceral origin). Study participants were re-evaluated after a week. If pain intensity was at least VAS 5, the dose of tramadol was increased to 200 mg twice daily. Patients were eligible for the next step if, despite medication, their persisting pain intensity was at least VAS 5 after the second week of treatment.

We tried to achieve a balanced study design by randomization. Patients were randomly allocated into the gabapentin group (Neurontin®, Goedecke AG, Berlin, Germany), the amitriptyline group (Saroten®, Lundbeck, Kopenhagen, Denmark) or the combination group. Treatments with metamizol and tra-

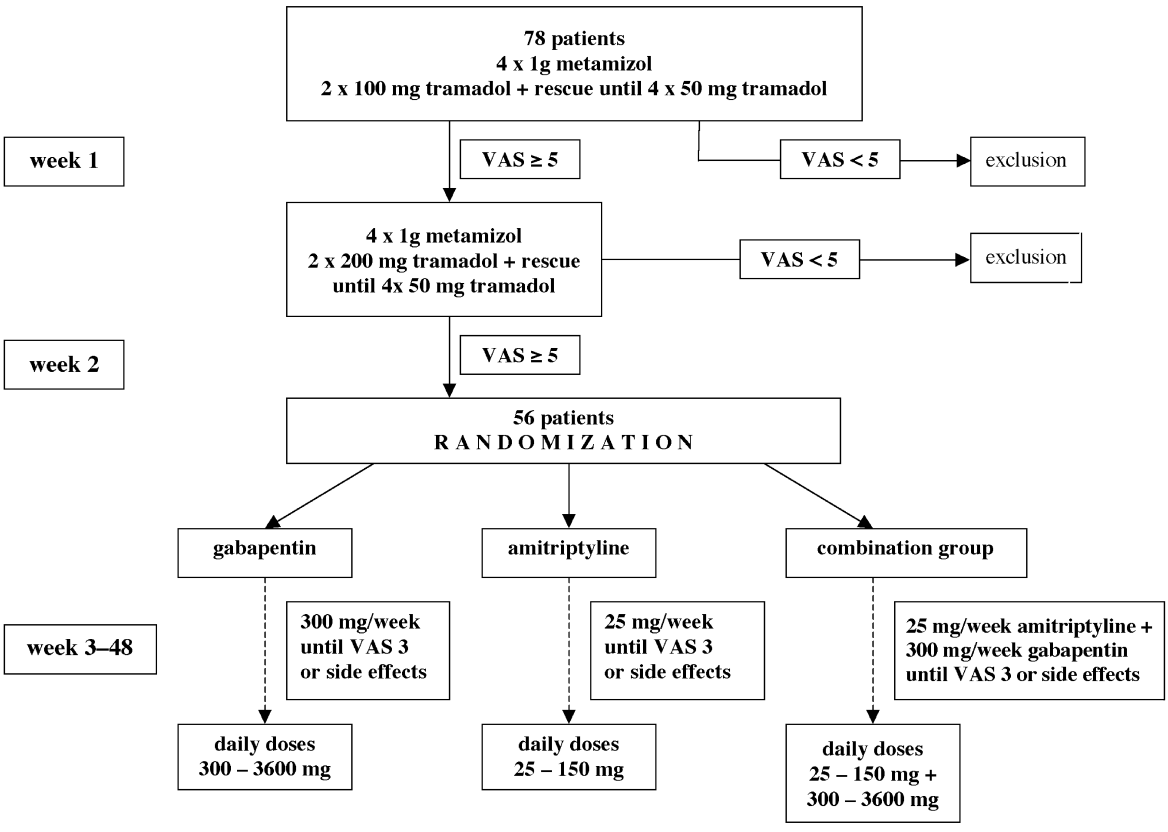

Fig. 1. Trial profile

madol were discontinued upon randomization. Exclusion criteria for antineuropathic treatment with amitriptyline and gabapentin were renal, hepatic, cardiovascular or psychiatric disorders. In order to avoid unwanted side effects, the dose of amitriptyline was carefully increased from an initial dose of 25 mg per day up to a maximum dose of 150 mg per day in 25 mg increments each week until sufficient pain relief, or the occurrence of side effects such as somnolence, dizziness, orthostatic hypotension, palpitations, dry mouth and weight gain. Similarly, the dose of gabapentin was carefully increased from 300 mg per day up to a maximum dose of 3600 mg per day in 300 mg increments each week until sufficient pain relief, or the occurrence of side effects such as dizziness, somnolence, edema and ataxia. Exclusion criteria were the concomitant administration of strong opioids, nonsteroidal anti-inflammatory drugs, benzodiazepines, capsaicin or skeletal muscle relaxants.

Intensity and quality of the pain and side effects of the medication were routinely evaluated at the weekly visit to the pain center for the first three months, and then at least once a month for 24 months. If pain relief was maintained for three months, doses of amitriptyline and gabapentin were carefully decreased and adjusted to maintain VAS below 3.

Demographic, social and economic data were documented. All patients also received active and passive physical therapy, transcutaneous electrical nerve stimulation and/or acupuncture at the beginning of the study. The use of adjuvant pain therapies was documented. Patients' overall satisfaction with their pain treatment was determined at the end of the study period.

Statistical analysis

Data are presented as means ± standard deviation (SD) or as counts and percent of total. *P*-values < 0.05 were considered to be statistically significant. In a preliminary analysis the differences from baseline values were tested against being different from zero at each time-point in each of the three treatment groups. For this purpose, a repeated measurements analysis of variance was performed with differences from baseline as outcome and age as a covariate for adjustment. The resulting 15 *P*-values were rigorously corrected using the method of Bonferroni-Holm. For the main analysis, i.e. for assessing the differences of VAS levels between groups at the five time-points, an analysis of covariance for repeated measurements was performed, with covariate age, and also with the baseline value as covariate. Time-specific group comparisons were corrected for multiplicity using a two-step procedure. The overall contrast of all three pair-wise group comparisons was computed for each of the five time-points, and the five resulting *P*-values were corrected by the Bonferroni-Holm method. For each time-point that was considered significant in this way, the three separate group comparisons were computed without further correction (Fisher's LSD principle). For both drugs, the dose pattern over time was assessed using the Cochran-Mantel-Haenszel statistic (test against non-zero correlation over strata) based on rank scores and stratified for treatment groups. For the time-points 12 and 24 months of treatment, the number of different pain qualities was compared between treatment groups using the Kruskal-Wallis test, stratified for the number of different pain qualities before treatment. At baseline and at 12 and 24 months, the incidences of each single pain quality were compared between treatment groups using Fisher's exact test. The incidences of side effects were compared at each time-point by a comparison between all three treatment groups of the incidence that any side effect occurred (Fisher's exact test); a Bonferroni-Holm correction was performed for the five time-points and corrected *P*-values are given. For overall tests that were significant after this correction, the three pair-wise comparisons were computed (again using Fisher's exact test) without further correction.

SAS Version 8.2 (SAS Institute Inc., Cary, NC, USA, 2001) was used for all computations.

Results

Patient enrolment

Seventy-eight patients with chronic pelvic pain entered pain therapy at our pain clinic. In 56 patients, pain intensities persisted above VAS 5 after the first two weeks of treatment with metamizol and tramadol. There was no significant difference in pain history and demographic data between patients with VAS > 5 and those with VAS < 5. In the 56 patients with greater pain intensity, metamizol and tramadol were replaced by gabapentin (n = 20), amitriptyline (n = 20), or a combination of both drugs (n = 16) (Fig. 1). During the study period of 24 months, seven patients discontinued pain treatment: in the gabapentin group, one patient was not compliant and two experienced severe side effects which necessitated discontinuation of oral medication; in the amitriptyline group, one patient dropped out because of insufficient pain reduction and two experienced severe side effects; in

Table 1. Demographic and socioeconomic data

	AMI (N = 20)	GBP (N = 20)	AMI/GBP (N = 16)
Age	36.7 ± 11.0 yrs	40.4 ± 12.9 yrs	49.6 ± 15.3 yrs
Weight	77.4 ± 14.0 kg	74.2 ± 11.7 kg	79.6 ± 12.3 kg
Height	169.7 ± 7.9 cm	170.8 ± 8.3 cm	169.9 ± 6.8 cm
Stable partnership	10 (50%)	12 (60%)	11 (69%)
One child	6 (30%)	5 (25%)	6 (38%)
Two children	1 (5%)	4 (20%)	3 (19%)
Three children	2 (10%)	1 (5%)	1 (6%)
Retired	1 (5%)	1 (5%)	2 (13%)
On sick leave	7 (35%)	6 (30%)	6 (38%)
Working full time	9 (45%)	7 (35%)	8 (50%)
Unemployed	0 (0%)	1 (5%)	0 (0%)

Data are presented as means ± SD or as numbers (percent of totals). *AMI* amitriptyline, *GBP* gabapentin.

Table 2. Patients' characteristics

		AMI	GBP	AMI/GBP
Location of pain	Vagina	5 (25%)	4 (20%)	1 (6.25%)
	Vulva	2 (10%)	2 (10%)	2 (12.5%)
	Anus	2 (10%)	1 (5%)	2 (12.5%)
	Perineum	1 (5%)	0 (0%)	20 (12.5%)
	Sacral	2 (4%)	4 (20%)	1 (6.25%)
	Right lower abdomen	9 (45%)	11 (55%)	8 (50%)
	Left lower abdomen	7 (35%)	6 (30%)	3 (19%)
	Middle lower abdomen	13 (65%)	7 (35%)	10 (63%)
Cause of pain	Hysterectomy	6 (30%)	6 (30%)	5 (31.25%)
	Pelvyplasty	1 (5%)	1 (5%)	1 (6.25%)
	Bladder distension	1 (5%)	1 (5%)	0 (0%)
	Herniotomy	*1 (5%)*	*1 (5%)*	*1 (6.25%)*
	Appendectomy	7 (35%)	4 (20%)	7 (43.75%)
	Intestinal surgery	1 (5%)	2 (10%)	1 (6.25%)
	Urogenital infection	9 (45%)	6 (30%)	5 (31.25%)
	Sexual abuse	1 (5%)	3 (15%)	2 (12.5%)
Prior surgery	Once	8 (40%)	6 (30%)	2 (12.5%)
	Twice	2 (10%)	5 (10%)	1 (6.25%)
	Three times or more	6 (30%)	5 (25%)	7 (43.75%)
Concomitant disease				
Low back pain	with MRI-verified pathology	7 (36%)	5 (25%)	5 (31.3%)
Irritable bowel syndrome		6 (30%)	3 (15%)	5 (31.3%)
Adjuvant pain therapies				
TENS		16 (80%)	16 (80%)	13 (81.3%)
Acupuncture		6 (30%)	6 (30%)	3 (18.75%)
Psychotherapy	Prior treatment	1 (5%)	5 (25%)	1 (6.25%)
	After 12 months	17 (100%)	16 (100%)	15 (100%)
	After 24 months	10 (58.82%)	10 (62.5%)	9 (60%)

Data are presented as numbers (percent of totals). *AMI* amitriptyline; *GBP* gabapentin; *MRI* magnet resonance imaging; *TENS* transcutaneous electrical nerve stimulation.

the combination group, one patient experienced severe side effects. Accordingly, 49 of the 56 patients were included in the final data analysis.

Demographic and socio-economic data

At the time of enrolment, there were no relevant differences in age, weight, height or socio-economic status between the three treatment groups (Table 1).

Pain history

Mean duration of pain before enrolment was 5.9 ± 2.4 years, without any difference between the three groups. The majority of patients had experienced various treatments before entering our study, including analgesic drugs, trigger-point infiltrations, transcutaneous electrical nerve stimulation, as well as both active and passive physiotherapy including massage, warmth and galvanization. During the study period of 24 months, all patients received active and passive physiotherapy and psychotherapy (Table 2). The location of pain (abdomen, perineum, anus, vulva, vagina or low back) and the mean number of prior surgical interventions were similar in all groups (Table 2).

Effects of antineuropathic therapy on the intensity and quality of pain

The course of pain intensity is shown in Fig. 2. There was no difference between the groups in the initial VAS score (gabapentin group 7.7 ± 1.5, amitriptyline group 7.3 ± 1.5, amitriptyline/gabapentin group 7.6 ± 0.8). All patients experienced significant pain relief at all investigated time-points compared with the pain score before treatment (all uncorrected P-values < 0.0001). However, after 6, 12 and 24 months, pain relief was significantly greater in patients receiving gabapentin either alone or in combination with amitriptyline than in patients on amitriptyline alone.

The mean daily doses of antineuropathic drugs required for pain relief in the absence of side effects were decreased after three months, within the first six months of treatment (Table 3). In all groups, dosages could be reduced over time until 24 months of treatment. There was a significant negative correlation between time and dosage (amitriptyline $P = 0.003$, gabapentin $P < 0.001$).

At 24 months of antineuropathic pharmacotherapy, there was no significant difference between the groups in the number of different pain qualities corrected for base-

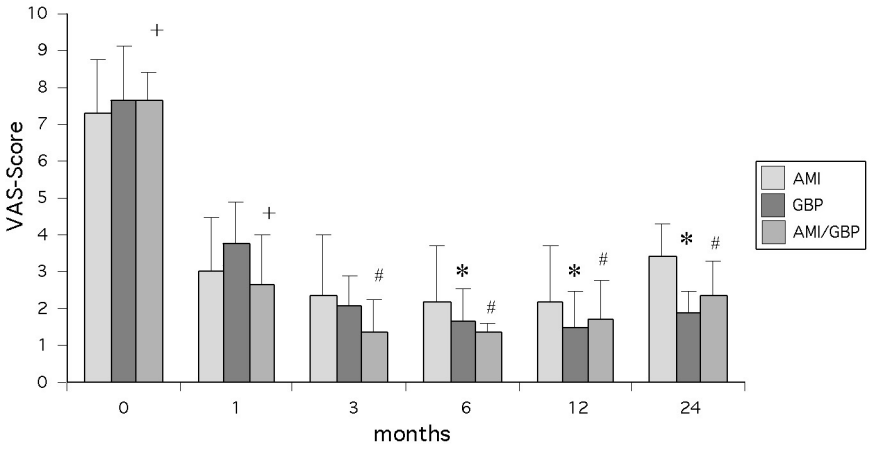

Fig. 2. Pain intensity under gabapentin (GBP), amitriptyline (AMI) and their combination. Data are presented as means ± SD of subjective visual analog scales (VAS) scores ranging from 0 (= no pain) to 10 (= worst pain imaginable). * AMI group versus GBP group; # AMI group versus AMI/GBP group, and GBP group versus AMI/GBP group, significant at the 5% level (corrected for multiplicity)

line values ($P = 0.112$); however, the same analysis showed a significantly different number of pain qualities after 12 months ($P = 0.018$). There was no group difference in the incidences of single pain qualities at the different time-points (baseline, 12 and 24 months) (Table 4).

Side effects of antineuropathic therapy

The incidences of side effects are shown in Fig. 3. The incidence of minor side effects which prevented a further increase in the daily drug dosage was lower in the gabapentin group than in the two other groups throughout the observation period (corrected *P*-values for the overall three-groups comparison at 1, 3, 6, 12, 24 months: 0.071, 0.024, 0.067, 0.115, 0.115). There was no significant difference between the groups in the incidence of severe side effects, requiring discontinuation of treatment (gabapentin n = 2; amitriptyline n = 2; amitriptyline/gabapentin n = 1).

Discussion

In the present study the therapeutic effects of gabapentin, amitriptyline, and the combination of amitriptyline/gabapentin were compared in 56 adult female patients with chronic pelvic pain refractory to surgical intervention and antinociceptive pharmacotherapy with metamizol and tramadol. All patients experienced signifi-

Table 3. Mean daily doses of antineuropathic drugs

Treatment duration	AMI	GBP	AMI/GBP
1 month	59.23 ± 23.52 mg (10–100)	1559.00 ± 524.63 mg (600–2400)	75.50 ± 33.91 mg (10–150) 1487.50 ± 586.37mg (900–3200)
3 months	63.89 ± 19.56 mg (25–100)	1788.24 ± 427.02 mg (1200–2400)	76.67 ± 30.56 mg (10–150) 1473.33 ± 113.59 mg (900–2400)
6 months	66.18 ± 17.55 mg (25–100)	1731.25 ± 442.29 mg (900–2400)	65.00 ± 18.41 mg (25–150) 1393.33 ± 361.48 mg (900–1800)
12 months	42.65 ±17.15 mg (25–75)	1287.50 ± 537.74 mg (600–2400)	66.67 ± 22.49 mg (25–125) 886.67 ± 718.99 mg (0–1800)
24 months	52.94 ± 24.82 mg (0–75)	925 ± 798.75 mg (0–2400)	40.0 ± 36.35 (0–75) 480.0 ± 421.22 (0–1200)

Data are presented as means ± SD and range (minimum–maximum). *AMI* amitriptyline, *GBP* gabapentin.

Table 4. Pain qualities

Pain quality	At beginning			12 months			24 months		
	AMI	GBP	AMI/GBP	AMI	GBP	AMI/GBP	AMI	GBP	AMI/GBP
Burning	14 (70%)	9 (45%)	8 (50%)	3 (12%)	2 (10%)	0 (0%)	3 (15%)	0 (0%)	3 (15%)
Lancinating	10 (50%)	9 (45%)	8 (50%)	3 (15%)	1 (5%)	1 (6.3%)	3 (15%)	1 (5%)	1 (6.3%)
Searing	3 (15%)	1 (5%)	4 (25%)	6 (30%)	3 (15%)	1 (6.3%)	1 (5%)	0 (0%)	2 (12.5%)
Electrifying	3 (15%)	6 (30%)	4 (25%)	2 (10%)	0 (0%)	0 (0%)	2 (10%)	0 (0%)	0 (0%)
Aching	9 (45%)	9 (45%)	2 (12.5%)	0 (0%)	0 (0%)	1 (6.3%)	6 (30%)	4 (20%)	1 (6.3%)
Cramps	5 (25%)	6 (30%)	5 (31.25%)	0 (0%)	0 (0%)	0 (0%)	3 (15%)	0 (0%)	1 (6.3%)

Fisher's exact test: all uncorrected P > 0.06. *AMI* amitriptyline; *GBP* gabapentin.

cant pain relief during the observation period of 24 months; however, pain relief was significantly greater in patients receiving gabapentin either alone or in combination with amitriptyline than in patients on amitriptyline alone. To our knowledge, this is the first study to compare the efficacy of the antineuropathic drugs gabapentin and amitriptyline in women with chronic pelvic pain. In contrast to our results, a study in diabetic patients with neuropathic pain found that gabapentin and amitriptyline gave similar degrees of pain relief [16], although others have also observed the superiority of gabapentin over amitriptyline in diabetic neuropathic pain [17].

A few studies have compared amitriptyline versus placebo and gabapentin versus placebo in patients with chronic pelvic pain [18, 19]. Amitriptyline has been recommended as the treatment of choice by some authors [11], whereas others have reported disappointing results [12]. Similarly, gabapentin failed to improve genitourinary-tract pain in some studies [19], but has been proven successful in the treatment of diabetic neuropathy, postherpetic neuropathy, neuropathic pain associated with carcinoma, multiple sclerosis, genitourinary-tract pain and vulvodynia by others [20]. Although spontaneous, paroxysmal pain of burning or lancinating quality and allodynia to cold and tactile stimuli respond to gabapentin, dull, aching pain and hyperalgesia are less likely to do so. Our study confirms that chronic pelvic pain has typical qualities of neuropathic pain conditions: these include the persistent burning and convulsive quality of the pain, allodynia and hyperpathia, as well as the frequent absence of morphological pathology. The genesis of neuropathic pain seems to be complex, involving both peripheral and central nervous mechanisms [13, 21, 22]. Peripheral nerves generate ectopic discharges by increasing the activation of sodium channels [6, 12, 13], and this process is likely to be responsible for spontaneous, paroxysmal pain in neuropathy. The activation of N-methyl-D-aspartate (NMDA) receptors and an imbalance between the inhibitory and excitatory circuitry at the spinal level contribute to central sensitization of the spinal cord dorsal-horn neurons in response to abnormal, repetitive peripheral nociceptive inputs following nerve or tissue injury [12]. Central sensitization plays a key role in both the development and maintenance of neuropathic pain symptoms [12, 13]. In our patients, gabapentin was more effective than amitriptyline in ameliorating neuropathic burning or spontaneous, paroxysmal pain. Interestingly, the effect of gabapentin does not seem to interact with any of these known mechanisms of neuropathic pain [12, 13]. Further studies are required to determine which mechanisms are involved in the genesis of chronic pelvic pain and at which site gabapentin and amitriptyline exert their pain-relieving effect, as demonstrated by our results and by others [17–19, 21].

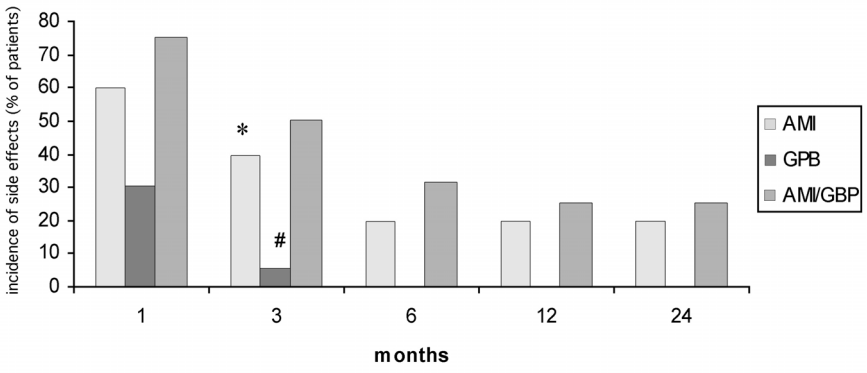

Fig. 3. Side effects of gabapentin (GBP), amitriptyline (AMI) and their combination. Side effects that prevented a further increase in the daily drug dosage were lower in the gabapentin group than in the two other groups throughout the observation period, and significantly lower after 3 months. Data are presented as means ± SD. * AMI group versus GBP group; # GBP group versus AMI/GBP group, significant at the 5% level (corrected for multiplicity)

In our study, first-line treatment with metamizol and tramadol was insufficient in 72% of all patients entering pain therapy, indicating that conventional antinociceptive therapy including non-opioid drugs and weak opioids is insufficient in most patients with chronic pelvic pain. Tricyclic antidepressants have been used in the treatment of many pain syndromes and have been shown to improve pain tolerance, restore normal sleep and reduce depressive symptoms [4, 24]. First-generation antiepileptic drugs have been shown to be effective in neuropathic pain [25], and evidence supporting the use of a new generation of antiepileptic drugs in neuropathic pain has been reviewed. However, without head-to-head comparisons between antidepressants and other analgesics, it is not possible to provide evidence-based treatment algorithms for neuropathic pain. The neuropathic component of chronic pelvic pain needs to be acknowledged before (invasive) antinociceptive strategies are considered. Our data also show that neither the anticonvulsant drug gabapentin nor the antidepressant drug amitriptyline could completely relieve pain. A combination of gabapentin and morphine achieved better analgesia at lower doses of each drug than either as a single agent, but with constipation, sedation and dry mouth as the most frequent adverse effects [25, 26]. Considering the co-existence of nociceptive causes of pain, a combination of antineuropathic agents together with nonsteroidal anti-inflammatory drugs and/or opioids and placebo should be examined in a further prospective study.

When choosing medication, efficacy and safety profiles are usually considered [27]. Although effective, both gabapentin and amitriptyline may exert significant side effects such as sedation, lethargy, weakness, dizziness, dry mouth, visual disturbance, tinnitus and palpitations, which often limit their clinical use [26, 27]. In order to minimize side effects, we slowly increased the daily dose up to a maximum dose of 3600 mg gabapentin and 150 mg amitriptyline [17, 19], and the rates of severe side effects necessitating discontinuation of oral medication were similar in the two drugs. In agreement with a previous study [17], gabapentin had a significantly lower rate of mild side effects than amitriptyline and the gabapentin side effects decreased during the follow-up period [20]. Dosages of both drugs could be reduced during the first year of antineuropathic treatment.

Chronic pain often leads to emotional suffering, functional impairment and social withdrawal [29, 30]. The improvements in socioeconomic parameters in our patients indicate the potential of antineuropathic therapy to improve quality of life and thus reduce medical health costs and the economic burden for society.

In conclusion, our study shows that chronic pelvic pain in many women may be treated sufficiently, although not completely, with gabapentin and amitriptyline. Gabapentin alone produced fewer side effects than amitriptyline or combined amitriptyline/gabapentin. These findings should be pursued in a further, larger-scale study.

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Correspondence: Univ.-Prof. Sabine Sator-Katzenschlager, M.D., Department of Anesthesiology and Intensive Care (B), Pain Clinic, Währinger Gürtel 18–20, 1090 Vienna, Austria,
E-mail: sabine.sator-katzenschlager@meduniwien.ac.at